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Efficacy of Cooling Centers for Mitigating Physiological Strain in Older Adults during Daylong Heat Exposure: A Laboratory-Based Heat Wave Simulation

Robert D. Meade,[1,2] *Sean R. Notley,*[1] *Ashley P. Akerman,*[1] *James J. McCormick,*[1] *Kelli E. King,*[1] *Ronald J. Sigal,*[1,3,4,5,6] *and Glen P. Kenny*[1,6]

[1]Human and Environmental Physiology Research Unit, School of Human Kinetics, University of Ottawa, Ottawa, Ontario, Canada
[2]Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts, USA
[3]Department of Medicine, Faculties of Medicine and Kinesiology, University of Calgary, Calgary, Alberta, Canada
[4]Department of Cardiac Sciences, Faculties of Medicine and Kinesiology, University of Calgary, Calgary, Alberta, Canada
[5]Department of Community Health Sciences, Faculties of Medicine and Kinesiology, University of Calgary, Calgary, Alberta, Canada
[6]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

Background: Health agencies, including the U.S. Centers for Disease Control and Prevention and the World Health Organization, recommend that heat-vulnerable older adults without home air-conditioning should visit cooling centers or other air-conditioned locations (e.g., a shopping mall) during heat waves. However, experimental evidence supporting the effectiveness of brief air-conditioning is lacking.

Objective: We evaluated whether brief exposure to an air-conditioned environment, as experienced in a cooling center, was effective for limiting physiological strain in older adults during a daylong laboratory-based heat wave simulation.

Methods: Forty adults 64–79 years of age underwent a 9-h simulated heat wave (heat index: 37°C) with (cooling group, $n = 20$) or without (control group, $n = 20$) a cooling intervention consisting of 2-h rest in an air-conditioned room (~ 23°C, hours 5–6). Core and skin temperatures, whole-body heat exchange and storage, cardiovascular function, and circulating markers of acute inflammation were assessed.

Results: Core temperature was 0.8°C (95% CI: 0.6, 0.9) lower in the cooling group compared with the control group at the end of the cooling intervention ($p < 0.001$; hour 6), and it remained 0.3°C (95% CI: 0.2, 0.4) lower an hour after returning to the heat ($p < 0.001$; hour 7). Despite this, core temperatures in each group were statistically equivalent at hours 8 and 9, within ± 0.3°C ($p \leq 0.005$). Cooling also acutely reduced demand on the heart and improved indices of cardiovascular autonomic function ($p \leq 0.021$); however, these outcomes were not different between groups at the end of exposure ($p \geq 0.58$).

Discussion: Brief air-conditioning exposure during a simulated heat wave caused a robust but transient reduction in core temperature and cardiovascular strain. These findings provide important experimental support for national and international guidance that cooling centers are effective for limiting physiological strain during heat waves. However, they also show that the physiological impacts of brief cooling are temporary, a factor that has not been considered in guidance issued by health agencies. https://doi.org/10.1289/EHP11651

Introduction

The planet is warming at an unprecedented rate,[1] giving rise to more frequent and severe heat waves and increasing yearly heat-related fatalities.[2] Older adults (≥65 years of age) are among the most affected; global heat-related mortality in this demographic has increased 81% from the 2000–2005 average, reaching a record 345,000 deaths in 2019.[2] The increased risk in older adults has been ascribed to age-associated deterioration of body temperature regulation and cardiovascular function, leading to dangerous elevations in body core temperature, circulatory strain, and systemic inflammation during heat exposure, which increase the risk for numerous adverse health outcomes (e.g., heat stroke, major adverse cardiovascular events, acute kidney injury).[3] Developing evidence-based guidance on effective interventions for alleviating the physiological burden of extreme heat in vulnerable populations, such as the elderly, is a public health priority.[4]

Household air-conditioning provides highly effective protection from extreme heat but is cost-prohibitive and inaccessible to many.[4] National and international health agencies, including the U.S. Centers for Disease Control and Prevention (CDC)[5] and the World Health Organization (WHO)[6] widely recommend that individuals without home air-conditioning spend at least 1–3 h/d in an air-conditioned location (e.g., a cooling center, an air-conditioned shopping mall) to help cool the body during heat waves. However, a recent systematic review by the CDC found no direct evidence linking cooling centers with reduced mortality or morbidity.[5] This was attributed to challenges surveilling their usage and the unpredictable nature of extreme heat.[5] Recommendations on the use of cooling centers are instead based on case–control studies demonstrating that older adults who visited cooled locations during heat waves were up to 66% less likely to die of heat-related causes.[7,8] However, the observational nature of these reports makes it difficult to ascribe this effect to body cooling because there may be important confounders of the relation between cooling center use and protection from heat. Prognostic factors for heat-related mortality, such as physical or psychological health issues and the availability of social support,[7,8] also influence whether an individual engages in cooling behaviors, such as visiting a cooling center or other cooled location.[9]

Cooling centers are also recommended on the logic that moving from the heat to a cooler environment prevents adverse health events by lessening hyperthermia and the associated physiological burden.[5] The WHO further suggests that "even a few hours spent in an air-conditioned place can help [a person's] body stay cooler when [they] go back into the heat."[6] To our knowledge, however, the acute effects of brief air-conditioning exposure on physiological burden have not been evaluated experimentally, nor has the extent to which any cooling effect persists following return to the heat. Addressing these knowledge gaps would

Address correspondence to Glen P. Kenny, University of Ottawa, School of Human Kinetics, 125 University, Montpetit Hall, Room 367, Ottawa, Ontario, Canada, K1N 6N5. Telephone: (613) 562-5800 ext. 4282. Email: gkenny@uottawa.ca

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provide critical empirical evidence for the presumed physiological effects of cooling centers cited by health agencies, and mechanistic support for the epidemiological reports on which current recommendations are based.

Laboratory-based heat wave simulations are an emerging tool for assessing the efficacy of personal cooling interventions.[4] By evaluating whether interventions are effective for reducing surrogate physiological indicators linked with adverse health outcomes under environmental conditions comparable to those experienced during heat waves, these trials can be used to complement traditional forms of public health research to inform guidance,[4] especially where, as in the case of cooling centers, direct assessments have proven difficult.[5,7] We therefore designed this 9-h heat wave simulation to evaluate the efficacy of cooling centers for limiting excessive rises in core temperature and the accompanying physiological burden in older adults.

Our primary objective was to assess the effect of a midday cooling center intervention consisting of a 2-h exposure to an air-conditioned environment on body core temperature, both during the cooling period and following subsequent return to the heat. We hypothesized that core temperature would be lower in the cooling group compared with the control group following cooling, but comparable in each group by the end of the simulated heat wave. This is because body temperature is regulated through negative feedback control of heat exchange (via cutaneous vasodilation and sweating).[3] Maintaining a stable core temperature in a hot environment necessitates that whole-body heat loss increases to an extent sufficient to offset the combined rate of metabolic and environmental heat gain, which in turn requires a proportional increase in body temperature.[10,11] Any cooling experienced when visiting a cooling center or other cooled location would therefore suppress heat loss, meaning that, upon reentry to the hot environment, heat would be steadily gained until body temperatures rose to an extent sufficient to activate heat loss and reattain heat balance and stable core temperature.[12,13] Consistent with our primary hypothesis, we also posited that any effect of cooling on cardiovascular responses and acute circulating inflammatory markers would be abated by the end of the simulated heat wave.

Methods

Participants

This single-site, parallel groups, laboratory-based study (ClinicalTrials.gov identifier: NCT04353076) was approved by the University of Ottawa Health Sciences and Science Research Ethics Board (H-11-18-1186) and was conducted in accordance with the Declaration of Helsinki. Written and informed consent was obtained from all participants.

Participants were recruited from the Ottawa–Gatineau area in Ontario, Canada via community outreach (i.e., visits to community centers) and local email lists (e.g., through the National Association of Federal Retirees). Of the 73 individuals screened for enrollment, 40 adults 64–79 years of age who met the eligibility criteria participated between February 2019 and April 2021 (the flow of participants through the study is outlined in Figure S1 in the supplemental materials). Each was sequentially assigned to a 9-h heat wave simulation with (cooling group, $n = 20$) or without (control group, $n = 20$) midday cooling center intervention.

Prospective participants were eligible if they were 60–80 y old, nonsmoking, spoke English or French, and were able to provide informed consent (both males and females were eligible). Exclusion criteria included physical restriction (e.g., due to disease: intermittent claudication, renal impairment, active proliferative retinopathy, unstable cardiac or pulmonary disease, disabling stroke, severe arthritis), use of or changes in medication judged by the patient or investigators to make participation inadvisable, arterial blood pressure of >150 mmHg systolic or >95 mmHg diastolic as measured in a sitting position or current antihypertensive medication use, and cardiac abnormalities or symptoms identified in screening. Subject age, smoking status, physical restrictions, and medication use were evaluated through participant self-report. Cardiac abnormalities and symptoms were assessed in preliminary screening (described below in the "Preliminary Screening" section).

Participants self-reported being sedentary or habitually active. None had been previously diagnosed with conditions known to impact physiological responses to heat exposure, including diabetes mellitus, hypertension, heart disease, or kidney disease.[3] Reported medications included topical creams, ointments, and so on ($n = 8$), antidepressants ($n = 6$), statins ($n = 5$), hormone replacement ($n = 3$), and medications treating glaucoma ($n = 6$), benign prostatic hyperplasia ($n = 5$), gastrointestinal reflux ($n = 5$), hypothyroidism ($n = 4$), restless leg syndrome ($n = 2$), osteoporosis ($n = 2$), overactive bladder ($n = 1$), pain (as required, $n = 1$), and sleep disturbances ($n = 1$). Except for the antidepressants, none of the medications have been suggested to impair thermoregulatory responses to heat stress.[3] For the five participants taking antidepressants (one participant was taking two classes), dosages and reported side effects (both by participants and in the literature) did not make participation unadvisable (as judged by coauthor R.J.S., who is a medical doctor). Nevertheless, we performed sensitivity analyses to evaluate the effect of medication usage on thermoregulatory responses to heat exposure (discussed below in the "Sensitivity analyses" section). No participants were currently smoking ($n = 24$ never smokers and $n = 16$ past smokers). All past smokers had quit ≥19 y prior to participation. All female participants were postmenopausal ($n = 16$).

Experimental Procedures

All participants completed a preliminary screening session and an experimental heat wave simulation trial. Testing was conducted at the Human and Environmental Physiology Research Unit of the University of Ottawa in Ottawa, Ontario, Canada. Ottawa has a temperate humid–continental climate characterized by warm, humid summers and cold winters.[14] Testing was confined to the fall, winter, and spring months. We opted to suspend testing in the summer because the health impacts of heat waves are more pronounced early in the summer, likely owing to a lack of natural acclimatization,[15] which occurs with seasonal elevations in heat exposure.[16,17] No testing was completed between March and November 2020 because of the COVID-19 pandemic.

Participants were instructed to avoid strenuous physical activity and alcohol for 24 h prior to preliminary and experimental sessions and to eat a light meal 2 h before the start of each session. Participants were also asked to consume a minimum of 500 mL of water the night before and morning of each session to ensure adequate hydration, which was verified upon arrival to the laboratory through a measurement of urine specific gravity. Adequate hydration was defined as a urine specific gravity of <1:025 (Reichert TS 400 total solids refractometer; Reichert).[18] If this threshold was exceeded, 400–500 mL of tap water was provided, and urine specific gravity was tested again after ∼30 min. Light summer clothing was worn for all sessions (sandals, shorts, and a light top for women).

Preliminary Screening

During the preliminary session, prospective participants were familiarized with all procedures and measurements and completed the Canadian Society for Exercise Physiology (CSEP),

Get Active Questionnaire (GAQ), and the American Heart Association (AHA) Pre-Participation Screening Questionnaire to assess their eligibility to participate (described above in the "Participants" section). The GAQ was also used to assess habitual activity levels along with the Kohl Physical Activity Questionnaire to determine the general types of physical activity performed.[19,20]

After completing the forms, resting arterial blood pressure was taken in triplicate (~30 s between measures) via manual auscultation of the brachial artery. Consistent with AHA guidance, participants were seated for at least 15 min before blood pressure measurement, resting quietly with both feet flat on the floor, and the cuff was placed at the approximate level of the left ventricle (fourth intercostal space).[21] Descriptive anthropomorphic data were then collected. Body height and mass were determined via a stadiometer (model 2391; Detecto) and a digital weighing terminal (model CBU150X; Mettler Toledo Inc.), respectively, and used to calculate body mass index and surface area.[22] Thereafter, participants performed an exercise stress test (semirecumbent cycling) to volitional fatigue. Participants were monitored via 12-lead echocardiogram by an American College of Sports Medicine and Canadian Society for Exercise Physiology–certified exercise physiologist (see the "Acknowledgments" section).

For trials completed after November 2020 (following resumption of testing after COVID-19–related lockdowns), initial screening was conducted over the phone and the Rose Angina Questionnaire (RAQ) was used to screen for cardiac symptoms[23] in place of the exercise stress test. Resting blood pressure and anthropomorphic data were collected in the morning of the heat wave simulation. To ensure consistency, reported anthropomorphic data in Table 1 are those measured at the start of the experimental trial.

Daylong Heat Wave Simulation

An overview of the procedures and measurements for the daylong heat wave simulation is presented in Figure 1. The heat wave simulations commenced between 0630 and 0900 hours. After arriving at the laboratory, participants dressed in light summer clothing, inserted a rectal temperature probe, and were instrumented with digital skin temperature sensors and a five-lead ECG (see the "Outcomes" section below for more detail).

Following instrumentation and baseline measurements (~2 h), participants entered a climate chamber regulated to a mean [standard deviation (SD)] heat index of 37°C [40.3 (0.1°C) air temperature and 9.3 (0.3)% relative humidity (RH)] with low airflow (<0.3 m/s) to begin the 9-h heat wave simulation. These conditions are similar to maximums recorded in North American and European cities,[4] although lower than peak conditions recorded during the 2021 heat dome event in the Pacific Northwest United States and Western Canada (daily peak conditions: 38.2–49.6°C, 9–20% RH, 37–44°C heat index).[24]

Participants spent the first 3 h (hours 1–3) seated within a modified Snellen air calorimeter, a unique device for directly measuring whole-body heat exchange, which is housed within the climate chamber.[25–27] The control group spent the next 3 h (hours 4–6) seated in the climate chamber (but outside the calorimeter). The cooling group spent hour 4 in the climate chamber but moved to an air-conditioned room for hours 5–6 (cooling center intervention: 23°C air temperature, 50% RH, <0.3 m/s airflow). Tap water (~16°C) was available *ad libitum* and participants could eat a light lunch during hours 4–6. At the 6-h mark, participants in the cooling group returned to the climate chamber and both groups spent the final 3 h of the simulation (hours 7–9) seated within the calorimeter. Participants were encouraged to use the washroom prior to each calorimeter measurement period. A portable urinal was provided for those in the control group so that participants could remain in the climate chamber. Participants unwilling or unable to use the portable urinal were allowed to leave the heat and use the laboratory washroom ($n=7$, maximum 5 min). For participants in the cooling group, washroom breaks occurred during periods where participants were not in the climate chamber.

Table 1. Participant characteristics and core temperature, cardiovascular outcomes, and acute inflammatory markers at baseline and during the initial heat exposure prior to the cooling center intervention.

	Control ($n=19$) [mean (SD) or n participants (%)][a]	Cooling ($n=19$) [mean (SD) or n participants (%)][a]
Participant characteristics		
Age (y)	72 (4)	71 (4)
Female (sex)	7 (37%)	9 (47%)
Height (cm)	170 (11)	168 (11)
Body mass (kg)	72.2 (11.3)	72.5 (11.3)
Body mass index (kg/m^2)[b]	25.1 (3.3)	25.7 (2.4)
Body surface area (m^2)[c]	1.83 (0.19)	1.82 (0.19)
Self-reported physical activity (min/wk)[d]	176 (154)	150 (115)
Types of physical activity[e]		
Walking	14 (74%)	14 (74%)
Jogging, biking, or swimming	9 (47%)	7 (37%)
Aerobics, floor exercises, or calisthenics	7 (37%)	4 (21%)
Organized sports	2 (11%)	6 (32%)
Taking prescription medications[f]	13 (68%)	11 (58%)
Core temperature, cardiovascular outcomes, and inflammatory markers prior to heat exposure [baseline (hour 0)]		
Core temperature (°C)	36.9 (0.2)	37.0 (0.3)
Mean skin temperature (°C)	31.9 (0.9)	31.3 (0.5)
Heart rate (bpm)	63 (8)	64 (10)
Rate pressure product (mmHg × bpm)	8,094 (1,509)	7,492 (1,443)
SDNN (ms)	39.9 (23.8)	37.6 (13.2)
RMSSD (ms)	31.0 (27.2)	25.3 (16.5)
Mean arterial blood pressure (mmHg)	93 (8)	86 (10)
Interleukin-6 (pg/mL)	5.80 (2.21)	6.01 (3.24)
Tumor necrosis factor-α (pg/mL)	11.60 (8.85)	13.12 (11.71)
C-reactive protein (mg/L)	0.35 (0.17)	0.38 (0.20)
Core temperature and cardiovascular outcomes prior to the cooling intervention[g]		
Core temperature (°C)	37.8 (0.2)	37.8 (0.3)
Mean skin temperature (°C)	36.3 (0.6)	36.4 (0.4)
Heart rate (bpm)	80 (14)	80 (13)
Rate pressure product (mmHg × bpm)	9,569 (2,114)	8,698 (1,826)
SDNN (ms)	42.5 (24.4)	40.0 (16.1)
RMSSD (ms)	23.9 (21.5)	18.0 (13.4)
Mean arterial blood pressure (mmHg)	85 (10)	81 (7)
Change in core temperature and cardiovascular outcomes over the initial heat exposure[g]		
Core temperature (°C)	0.9 (0.2)	0.8 (0.2)
Mean skin temperature (°C)	4.5 (0.9)	5.0 (0.6)
Heart rate (bpm)	17 (9)	16 (8)
Rate pressure product (mmHg × bpm)	1,475 (1,098)	1,206 (850)
SDNN (ms)	2.6 (22.3)	2.4 (11.7)
RMSSD (ms)	−7.1 (14.8)	−7.3 (6.8)
Mean arterial blood pressure (mmHg)	−7 (6)	−5 (8)

Note: RMSSD, root mean square of successive differences; SD, standard deviation; SDNN, standard deviation of successive normal-to-normal RR intervals.
[a]One participant in each of the control and cooling groups did not complete the entire simulation owing to symptoms of extreme hyperthermia and chest pains, respectively. Their characteristics are reported in the S1 Appendix. Data reported for are participants included in final analysis.
[b]Body mass index was calculated as weight in kilograms divided by the square of the height in meters.
[c]Body surface area was calculated according to the equation by Du Bois and Du Bois.[22]
[d]Weekly habitual physical activity quantified using the Get Active Questionaire.[19]
[e]Types of physical activity determined using the Kohl Physical Activity Questionnaire.[20]
[f]Reported medications included topical creams, ointments, and so on ($n=8$), antidepressants ($n=6$), statins ($n=5$), hormone replacement ($n=3$), and those treating glaucoma ($n=6$), benign prostatic hyperplasia ($n=5$), gastrointestinal reflux ($n=5$), hypoactive thyroid ($n=4$), restless leg syndrome ($n=2$), osteoporosis ($n=2$), overactive bladder ($n=1$), pain (as required, $n=1$), and sleep disturbances ($n=1$).
[g]Data presented for the last common measurement time point prior to the cooling center intervention: hour 4 for core temperatures and hour 3 for cardiovascular outcomes.

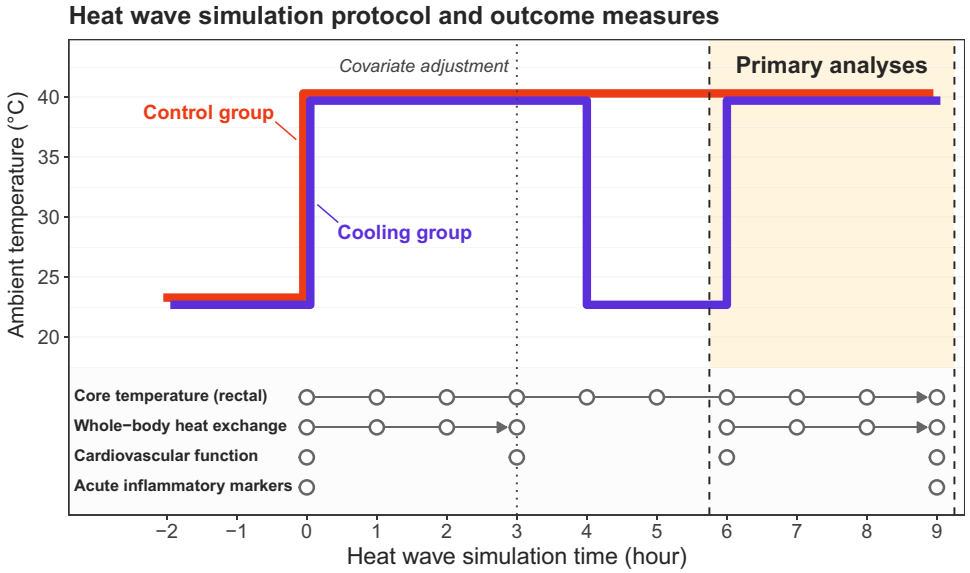

Figure 1. Overview of the heat wave simulation and timing of the outcome measurements. Participants in the control group (orange–red line) were exposed to a heat index of 37°C (40°C, 9% RH) for 9-h. Participants in the cooling group (blue–purple line) underwent the same procedures but spent hours 5–6 in an air-conditioned room (∼23°C, 50% RH). Core temperature was monitored continuously as the primary outcome. Whole-body heat exchange was measured during the first and final 3 h of exposure via direct calorimetry and used to quantify heat storage (amount of heat stored in the body). Cardiovascular function was evaluated in 3-h intervals, and markers of acute inflammation were measured prior to and at the end of the heat wave simulation. Physiological responses were compared between the control and cooling groups at the end of the cooling intervention and over 3 h following return to the heat (primary analyses) using linear mixed-effects models. Between-group comparisons were adjusted for the level of each outcome measured at the end of the initial heat exposure prior to cooling (covariate adjustment; akin to adjustment for baseline values) to account for variability stemming from measured and unmeasured individual modifiers of the physiological response to heat stress. Note: RH, relative humidity.

Outcomes

The following section details the measurement and analysis of study outcomes. Data were blinded prior to analysis by replacing each participant identifier in the name of the raw data files with a random file code. The author responsible for blinding data did not contribute to data analysis thereafter except to unblind the analyzed data.

Body core and skin temperatures. Visiting cooling centers or other cooled locations is recommended to help individuals maintain their body core temperature within safe limits when home air-conditioning is unavailable.[5,6] Rectal temperature was monitored as an index of core temperature using a general purpose thermocouple temperature probe (Mon-a-therm General Purpose Temperature Probe; Mallinckrodt Medical Inc.) inserted ∼12–15 cm past the anal sphincter. Data were collected in 15-s intervals using LabVIEW software (version 7.0; National Instruments). A temperature capsule (VitalSense ingestible capsule thermometer; Mini Mitter Company), which was ingested ∼2 h prior to the heat wave simulation, was used to monitor core temperature in place of the rectal thermocouple in three participants owing to technical difficulties ($n = 2$, control group) or participant refusal of the rectal thermocouple ($n = 1$, cooling group). Temperature data from the pill were recorded at 1 min intervals using a hip-worn recording device (VitalSense Monitor; Mini Mitter Company). These capsules demonstrate low systematic bias when assessed against rectal temperature.[28]

Skin temperature was assessed every minute using surface temperature monitors (DS1922L Thermochron; OnSolution Pty Ltd) affixed to eight body regions as described in ISO 9886:2004 using double-sided adhesives and medical tape.[29] Mean skin temperature was subsequently calculated based on the following weightings: 7% forehead, 17.5% right scapula, 17.5% upper left chest, 7% upper right arm, 7% right forearm, 5% left hand, 19% right anterior thigh, and 20% left calf.[29]

Core and skin temperature data were manually cleaned, interpolated (linear interpolation using the *na.approx* function of the *zoo package* for R[30]), and converted to 15-min averages at the end of each hour of heat exposure, except for at the end of hours 4 and 6. For these time points, temperatures were taken as the average of minutes 31–45 to accommodate the ∼5–10 min transition period between the climate chamber and air-conditioned room at the start and end of the cooling center intervention.

Whole-body heat exchange and storage. Elevations in core temperature occur when heat gain exceeds heat loss and heat is stored within the body. Whole-body heat gain (from metabolism and the environment) and heat loss (from sweat evaporation) were assessed to quantify body heat storage.[26] Whole-body dry and evaporative heat loss were measured during the first and final 3 h of the simulated heat wave (hours 1–3 and 7–9) via the Snellen air calorimeter, which provides the only direct measure of these variables.[25–27] Calorimeter inflow and outflow air temperature and absolute humidity were measured every 8 s with high-precision dew point hygrometers (model 373H; RH Systems) and resistance temperature detectors (Black Stack model 1560; Hart Electronics), respectively. Air mass flow, equivalent to <0.3 m/s where the participant was seated,[31] was determined via differential thermometry over a known heat source in the effluent air stream. All data were recorded with LabVIEW software (version 7.0; National Instruments).

Calorimeter inflow and outflow temperature and humidity data were smoothed using cubic splines (*smooth.spline* function of the *stats* package in base R). Minute averages for heat loss via sweat evaporation (evaporative heat loss) were then calculated using the smoothed outflow–inflow difference in absolute humidity, multiplied by air mass flow and the latent heat of vaporization of sweat (2,426 J/g). Dry heat loss was similarly derived from the smoothed outflow–inflow air temperature difference and specific heat capacity of air (1,005 J/kg/°C). Given that ambient temperature (∼40°C) was greater than that of the skin (∼35–36°C), dry heat loss was measured as a negative value and is referred to as dry heat gain hereafter.

While the participant rested within the Snellen air calorimeter, oxygen (O_2) and carbon dioxide (CO_2) exchange at the lungs was continuously measured using an automated indirect calorimetry system. Expired O_2 and CO_2 concentrations were measured with electrochemical gas analyzers (AMETEK models S-3A/1 and CD 3A; Applied Electrochemistry) from air drawn from a 6-L fluted mixing box located within the calorimeter. Expelled air was recycled back into the calorimeter chamber to account for respiratory heat exchange. The gas analyzers and turbine ventilometer were calibrated ~30 min prior to each of the two 3-h calorimetry measurement periods.

Derived values for O_2 and CO_2 exchange were smoothed with cubic splines (as above), converted to 1-min averages, and used to calculate metabolic rate.[26] Endogenous metabolic heat production (the rate of heat produced as a by-product of metabolism) was assumed to equal metabolic rate given that no external work was performed. Cumulative body heat storage (the amount of heat stored within the body) over each calorimeter measurement period (hours 1–3 and 7–9) was calculated as the temporal summation of whole-body heat gain (heat production + dry heat gain) – heat loss (evaporative heat loss).[26]

Cardiovascular function. Most heat-related fatalities are of cardiovascular origin, resulting from increased work placed on the heart to meet elevated circulatory demands and altered autonomic modulation.[3] Electrocardiogram (ECG) recordings during 10 min of seated rest were used to derive heart rate and two indices of heart rate variability (reflective of cardiac autonomic modulation). ECG data from the Holter monitor (DigiTrak XT Holter Monitor; Philips) were downloaded and analyzed using Philips Zymed software (version 3.0; Philips). RR interval data were extracted from the ECG tracing (3 channels at a sampling rate of 175 Hz) and normal-to-normal beats, as determined by the Zymed annotation algorithm, were retained for analysis.

Continuous individualized variability analysis (CIMVA) software was used to derive absolute heart rate and indices of heart rate variability (5-min windowed analysis with 30-s time step).[32] The latter included *a*) the SD of successive normal-to-normal intervals (SDNN), an index of overall variability; and *b*) the root mean square of successive differences (RMSSD), which is more reflective of short-term high frequency fluctuations in heart rate (mediated primarily by the parasympathetic nervous system).[33] Heart rate and heart rate variability data were smoothed with cubic splines (as above) and extracted at each of the four resting measurement periods occurring at ~3-h intervals during the heat wave simulation (hours 0, 3, 6, and 9; before and after each calorimetry period).

Arterial systolic and diastolic blood pressures were taken as the average of the three values measured at the brachial artery (~30 s between measures) via manual auscultation immediately following the 10-min resting ECG. During each measurement, participants rested quietly with both feet flat on the floor and the cuff at the approximate level of the left ventricle (fourth intercostal space), consistent with recommendations by the AHA.[21] Rate pressure product, an index of myocardial O_2 demand, was derived as heart rate × systolic pressure.[34,35] Systolic and diastolic pressures were also used to calculate mean arterial pressure (1/3 systolic+2/3 diastolic), which reflects the pressure regulated by the arterial baroreflex and is an index of organ perfusion pressure.[36]

Circulating markers of acute inflammation and plasma volume. Many heat-related injuries are linked to systemic inflammation.[3] We therefore assessed changes in circulating extracellular levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) during the 9-h heat wave simulations. These specific markers were chosen because they are commonly used to evaluate the acute inflammatory response,[37] have been linked to an increased risk of mortality in older adults,[38] and are implicated in the pathogenesis of adverse health outcomes common during heat waves, including heat stroke,[39,40] myocardial infarction,[41] and acute kidney injury.[42] Acute inflammatory markers were assessed in venous blood samples drawn from the antecubital vein at baseline and at the end of the heat wave simulation. Samples were transferred directly into Vacutainer tubes with potassium ethylenediaminetetraacetic acid (K_2EDTA; 3 mL of 7.2 mg K_2EDTA; BD) or no additive (5-mL SST Serum Separator Tube; BD). Hemoglobin and hematocrit were immediately measured in duplicate (Ac·T diff; Beckman Coulter) from whole blood (in a K_2EDTA tube) and used to estimate changes in plasma volume during the 9-h heat exposure.[43]

Blood in the tube without additive was left to clot for 20 min before centrifugation at 1.38 relative centrifugal force for 10 min (at room temperature). Separated serum was transferred into polypropylene Eppendorf tubes and stored at −80°C. Extracellular (serum) concentrations of IL-6 [DY206-05; Bio-Techne; limit of detection (LOD): 3.2 pg/mL], TNF-α (DY210-05; Bio-Techne; LOD: 4.0 pg/mL), and CRP (DY1707; Bio-Techne; LOD: 12.3 pg/mL) were later analyzed via enzyme-linked immunosorbent assay (ELISA) kits with provided ancillary reagents (DuoSet ELISA Ancillary Reagent Kit 2, DY008; Bio-Techne) according to the manufacturer's protocol. The sample to dilution ratio was 1:2 for IL-6 and TNF-α and 1:500 for CRP. Plates were read on a plate reader at a wavelength of 450 nm (Synergy; Biotek). Protein concentrations were corrected for the change in plasma volume during the heat wave simulation.

Statistical Analysis

Sample size determination. We performed *a priori* power analyses to determine the minimal sample size required to detect *a*) a ≥0.3°C difference in core temperature between the control and cooling groups using traditional null hypothesis significance testing, and *b*) statistical equivalence of core temperature within ±0.3°C using two one-sided tests,[44] with 80% power and $\alpha = 0.05$. The minimal effect size of interest and equivalence bounds (0.3°C) were selected based on the threshold for a clinically significant difference proposed in a trial assessing the effect of a common personal cooling intervention (electric fan use) on core temperature[45] and the typical day-to-day variation of core temperature.[46] The common SD (0.3°C) was determined from previous studies exposing middle-aged and older adults (55–73 years of age) to extreme heat conditions for 2–3 h.[47–49] A minimum sample size of 18 participants in each group was required based on the power analysis for the equivalence test, which gave the higher sample size of the two analyses (Figure S2 in the supplemental materials).

Following data collection, but prior to unblinding of the final outcome data, we adjusted our statistical analysis plan to improve efficiency and assess responses at multiple time points (correcting for multiplicity). We therefore performed a secondary analysis to determine how these decisions influenced power to detect statistical differences and equivalence between the control and cooling groups. These were conducted similarly to our *a priori* analyses, except α was reduced to 0.00625 to account for multiple comparisons (Bonferroni correction; described below in the section "Analysis of primary and secondary outcomes") and the pooled SD was set to 0.24°C based on a reanalysis of our previous study to reflect the new analyses. Specifically, SD was estimated from a linear mixed-effects (LME) model evaluating rectal temperature in older adults with and without type 2 diabetes, adjusting for baseline values, following 3-h of exposure to extreme heat stress (44°C air temperature, 30% RH). Based on these changes and the analyzed sample size ($n = 19$), our final analysis had ~82% power

to detect a $\geq 0.3^{\circ}C$ difference in rectal temperature between the control and cooling groups, and $\sim 76\%$ power to detect equivalence within $\pm 0.3^{\circ}C$, after multiplicity corrections (Figure S3). All sample size calculations were conducted using R statistical software (version 3.6.1; R Development Core Team).[44]

Missing data. In the final set of analyzed participants ($n = 38$; two participants did not complete the entire heat wave simulation; see the "Results" section), there were no missing data for the primary outcome, body core temperature, or for skin temperature, heart rate, rate pressure product, or arterial blood pressures. However, the following data for secondary measures are missing owing to technical difficulties with the recording equipment: $n = 3$ measurements of body heat storage ($n = 1$ in the control group and $n = 2$ in the cooling group), $n = 2$ measurements of SDNN and RMSSD ($n = 1$ in both control and cooling groups). In addition, difficulties with sample collection meant that venous blood samples were not collected for $n = 3$ participants ($n = 2$ in control and $n = 1$ in cooling group). We also removed extreme outliers for extracellular IL-6 and TNF-α ($n = 4$ participants in the control group had values greater than the 75th percentile+3 times interquartile range for both IL-6 and TNF-α).

We opted to not impute missing data and carried out analyses using the complete case approach. We felt this was appropriate given that missing data were missing primarily due to technical difficulties and could therefore be reasonably considered to be missing completely at random (i.e., there are no systematic differences between the missing and nonmissing data).[50] Under the missing-completely-at-random assumption, complete case analysis gives unbiased effect estimates.[50] Further, most of the missingness occurred in secondary outcome data. Techniques for estimating missing data, such as multiple imputation, can improve statistical power relative to the complete case approach when covariates are imputed (by allowing for participants with full data for the primary predictor and outcome but missing covariate data to be included in analysis),[51] but provide minimal benefit to power when the outcome is imputed.[52]

Analysis of primary and secondary outcomes. Study outcomes were analyzed using LME models. For the analysis of core temperature, mean skin temperature, and cardiovascular function, the fixed effects were experimental condition, time, and their interaction. The value of each outcome variable at the end of the first calorimetry measurement period (hour 3) was also included to adjust for individual variation in the response to the initial heat exposure prior to the cooling intervention. Heat storage over the final 3 h was analyzed similarly except that time was excluded from the model because this variable was expressed as a cumulative value (i.e., cumulative heat storage over the final 3 h was compared between groups after adjustment for heat storage over the first 3 h). The models for circulating inflammatory markers included experimental condition as a fixed effect, adjusted for participant sex and baseline values (inflammatory markers were not measured at the 3-h time point). Plasma volume was analyzed similarly, except that preexposure values were excluded from the model because this variable is necessarily presented as a change from baseline.[43] For all analyses, participant identification was modeled as a random effect. Akaike's information criterion was used to determine random effects and covariance structures.[53]

The model-derived estimated marginal means were compared between groups to evaluate the efficacy of the cooling intervention for attenuating physiological strain. We also assessed whether core temperature (primary outcome) was statistically equivalent in each group within $\pm 0.3^{\circ}C$ via two one-sided *t*-tests (performed on the model-estimated marginal means). Reported *p*-values and confidence intervals (CIs) were adjusted for multiplicity using the Bonferroni procedure. Null hypothesis significance tests and equivalence tests were considered part of the same family of tests. Although this approach is likely overly conservative,[54,55] we felt it was appropriate given the size of our trial. A two-sided $p < 0.050$ was considered statistically significant. Descriptive statistics are presented as means and SDs. Estimated between-group differences, which are corrected for values measured at the 3-h time point, are reported as means and 95% CIs (lower limit, upper limit). Analyses were conducted using R statistical software (version 3.6.1; R Development Core Team).[44,56–59]

Sensitivity analyses. We performed a series of sensitivity analyses to evaluate how key design factors and analytical decisions influenced the trials findings. To confirm the balance of the control and cooling groups with respect to the primary outcome, we compared body core temperature between groups at baseline and over the first 4 h of heat exposure, prior to the cooling center intervention, using an LME model with the fixed effects of time [5 levels: 0 (baseline), 1, 2, 3 and 4 h of heat exposure], condition, and their interaction. We then assessed whether core temperature was equivalent in each group using two one-sided tests.

Analysis of core and mean skin temperature, body heat storage, and cardiovascular markers were adjusted for values measured at the 3-h time point of the heat wave simulation. This covariate was included with the primary goal of reducing variability in the estimated impact of cooling stemming from measured and unmeasured individual modifiers of the physiological response to heat stress (e.g., sex, physical activity levels, medication use), akin to baseline adjustment in clinical trials.[60] In sensitivity analyses, we evaluated body core temperature in each group during and following the cooling intervention without adjusting for the 3-h time point to see how inclusion of this covariate impacted the studies primary findings.

Sex can modulate thermoregulatory function,[61] but its effect is most pronounced at higher levels of exercise-induced heat stress.[62,63] We therefore included both men and women in the study but did not evaluate sex-related differences in study outcomes due to concerns over insufficient statistical power to detect a sex × cooling × time interaction during resting heat exposure. As a simple method to assess the potential influence of participant sex on our findings, we compared between-group differences in core temperature over the first 4 h of exposure using an LME model, including time (hours 1–4) and sex and their interaction as fixed effects (baseline core temperature was included as a covariate). Although we did not enroll participants taking medications known to influence thermoregulatory function, we performed additional sensitivity analyses to determine the influence of general medication use (reporting any medication use vs. reporting no medication use) and use of antidepressants (reporting antidepressant use vs. not reporting antidepressant use) on the increase in core temperature over the first 4 h of heat exposure. Finally, a similar analysis was conducted to evaluate the influence of whether participants completed the heat wave simulation trials before or after the start of testing restrictions due to COVID-19 (i.e., before March 2020 or after November 2020) to evaluate the potential for selection bias introduced with changes in participant screening and enrollment procedures (described above).

Results

Participant Characteristics and Initial Physiological Responses to Heat Exposure

One participant in each of the control and cooling groups did not complete the entire heat wave simulation owing to symptoms of extreme hyperthermia and chest pain, respectively (their

characteristics are reported in Table S1 in the supplemental materials). The characteristics of the participants who completed the heat wave simulation are provided in Table 1, along with body temperatures, cardiovascular outcomes, and circulating extracellular acute inflammatory markers at baseline and during the initial period of heat exposure prior to cooling.

Body Temperatures and Heat Storage

At the end of the 2-h cooling center intervention, body core temperature was 0.8°C (95% CI: 0.6, 0.9) lower in the cooling group compared with the control group ($p < 0.001$; Figure 2). Although core temperature remained 0.3°C (95% CI: 0.2, 0.4) cooler in the cooling group an hour after returning to the heat ($p < 0.001$; hour 7), it was statistically equivalent between groups at the end of each of the subsequent 2 h ($p \leq 0.005$; hours 8–9).

Mean skin temperature was 4.2°C (95% CI: 3.9, 4.5) lower in the cooling group compared with the control group at the end of the cooling intervention ($p < 0.001$) but was 0.3°C (95% CI: 0.2, 0.5) higher in the cooling group an hour after returning to the heat ($p = 0.004$; Figure 2). Skin temperature was not different between groups at the end of the subsequent 2 h ($p > 0.99$). Body heat storage over the 3 h of heat exposure following cooling was 172 kg (95% CI: 113, 231) greater in the cooling group relative to the control group ($p < 0.001$; Figure 2).

Cardiovascular Function

Heart rate [cooling–control between-group difference: −10 (95% CI: −15, −6) bpm; $p < 0.001$] and rate pressure product [−793 (95% CI: −1480, −106) mmHg × bpm; $p = 0.021$] were lower, whereas SDNN [12.5 (95% CI: 6.1, 18.8) ms; $p < 0.001$] and RMSSD [5.4 (95% CI: 1.3, 9.4) ms; $p = 0.007$] were higher in the cooling group compared with the control group at the end of the cooling center intervention. No statistically significant between-group differences in these outcomes were observed at the end of the heat wave simulation (Table 2). Mean arterial blood pressure was not different between groups at any of the analyzed time points (Table 2).

Acute Inflammatory Response and Change in Plasma Volume

At the end of the 9-h heat wave simulation, no differences in circulating markers of acute inflammation were observed between the control and cooling groups (Table 3). Likewise, the change in plasma volume from basal levels to the end of exposure was not different between groups (Table 3).

Sensitivity Analyses

The core temperature response over the first 4 h of heat exposure prior to the cooling center intervention was statistically equivalent [within ±0.3°C in the control and cooling groups ($p \leq 0.005$; Table S3 and Figure S4 in the supplemental materials)]. Further, including responses measured at the 3-h time point of the heat wave simulation as a covariate did not impact the trials primary findings. Core temperature was still statistically lower in the cooling group compared with the control group at the end of the cooling intervention and an hour after returning to the heat but statistically equivalent in these groups over the final 2 h of the heat wave simulation ($p \leq 0.007$; Table S4). Finally, core temperature responses were not significantly influenced by participant sex ($p = 0.74$; Table S5 and Figure S5), whether participants reported taking prescription medications ($p = 0.51$; Table S6 and Figure S6), including antidepressants ($p = 0.78$; Table S7 and Figure S7), or the timing of participation relative to the beginning of the COVID-19 pandemic ($p = 0.26$; Table S8 and Figure S8).

Discussion

Older adults briefly exposed to air-conditioning during a daylong simulated heat wave experienced reduced body core temperature and lessened strain on the heart, evidenced by lower heart rate and rate pressure product and improved indices of cardiac autonomic modulation (SDNN and RMSSD), compared with a control group that remained in the heat for the entire 9 h. However, these benefits were transient; core temperature in participants exposed to the cooling intervention returned to levels equivalent to the noncooled control group within 2 h after returning to the heated environment. Although there is a need for larger, confirmatory studies, these findings provide important experimental support for national and international guidance that visiting cooling centers or other air-conditioned locations provides protection from heat stress and elevated physiological burden.[5,6] Further, our data lend mechanistic support for epidemiological reports indicating up to a 66% reduction in the odds of heat-related mortality in older adults who visited cooled locations during heat waves.[7,8] However, they also raise concerns over the transient physiological benefits of cooling centers, which have not previously been considered in guidance issued by health agencies.

Physiological Effects of Brief Ambient Cooling

Air-conditioning provides highly effective protection from extreme heat by cooling the ambient environment, facilitating passive heat transfer along the skin-to-environment temperature gradient.[4] However, home cooling is expensive and inaccessible to many heat-vulnerable persons,[64,65] including those in long-term care homes, public or congregate housing, and other facilities.[4,66] Air-conditioning is also energy intensive and can contribute to increasing greenhouse gas emissions (depending on the method of electricity generation and efficiency).[67,68] Recent guidance has therefore proposed the use of home-based cooling interventions, such as electric fans or skin dousing, as simple and sustainable alternatives to air-conditioning[4] on the basis of mild reductions in body core temperature (∼0.1°C)[45] and moderate attenuations in heart rate (∼4–8 bpm)[45,69] in young adults exposed to 2-h heat wave simulations. Because these interventions work by facilitating or supplementing evaporative cooling, they are less effective and, depending on environmental conditions, potentially detrimental in older adults owing to age-related reductions in sweat secretion.[70,71] For example, wearing a water-drenched shirt has been shown to lower core temperature by ∼0.2°C in older adults during a 2-h heat wave simulation (42°C, 34% RH).[70] However, that cooling effect is considerably smaller than the 0.8°C (95% CI: 0.6, 0.9) reduction in core temperature observed in the present study. It is also pertinent to note that, in contrast to visiting cooled locations, epidemiological data on the effectiveness of simple interventions such as fans, skin dousing, or taking extra showers, for preventing heat-related fatalities are equivocal.[7,8,72] That said, many of these low-cost strategies require little to no electrical input and could therefore be used during power outages (e.g., due to rolling blackouts, damage to electrical power infrastructure) or in low-resource settings[4] where the establishment of cooling centers is not feasible.

Core temperature remained 0.3°C (95% CI: 0.2, 0.4) lower in the cooling group an hour after the cooling intervention but was equivalent to the control group thereafter, likely due to the elevated storage of heat within the body over the final 3 h of the heat wave simulation in the cooling group (Figure 2). This finding was an expected consequence of the organization of the

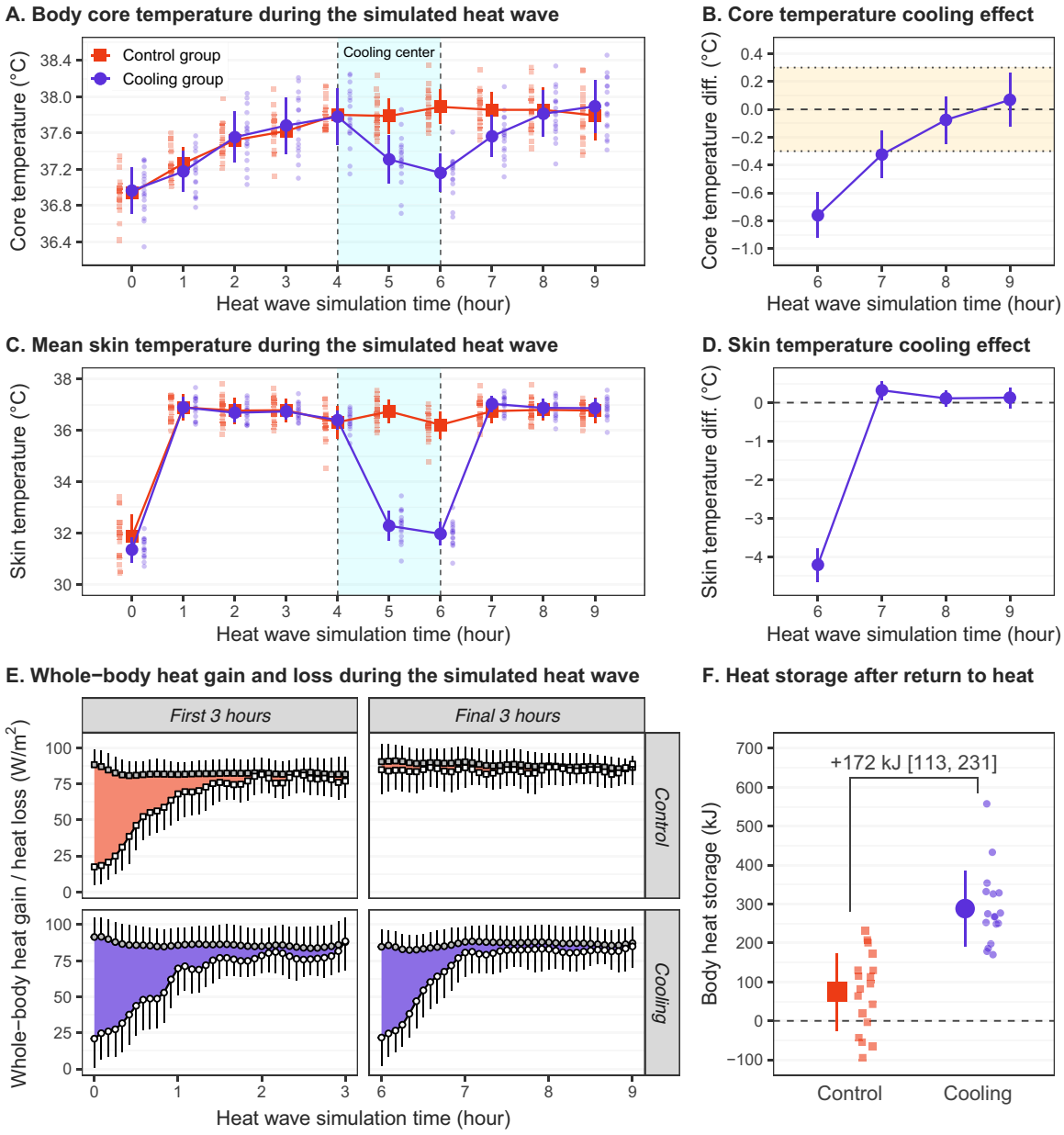

Figure 2. Effect of the cooling center intervention on body temperatures and heat storage. (A) Body core temperature (rectal) at the end of each hour of the 9-h heat wave simulation (heat index of 37°C; 40°C, 9% RH) in the control ($n = 19$; orange–red squares) and cooling groups ($n = 19$; blue–purple circles). The timing for the 2-h cooling center intervention (~23°C, 50% RH) is denoted by the blue shaded area. (B) Estimated mean difference in core temperature between the cooling and control groups (cooling–control, core temperature diff.). The gold shaded area denotes the zone of equivalence (if the presented CI falls completely within the area, core temperatures in each group were statistically equivalent within ±0.3°C). (C,D) Mean skin temperature presented in the same manner as core temperature (control: $n = 19$; cooling: $n = 19$). (E) Whole-body heat gain (heat gain due to metabolism and the environment, gray symbols) and heat loss (heat loss via sweating, white symbols) at 5-min intervals over the first and final 3 h of the heat event simulation. (F) Body heat storage over the final 3 h of exposure following the cooling center intervention (calculated as the temporal summation of heat gain and loss) in the control ($n = 18$) and cooling groups ($n = 17$). Missing data were not imputed. Absolute data (A,C,E,F) are presented as means (point estimates) and SD (error bars). Individual data (A,C,F) are shown as small symbols. Differences between groups (B,D,F) are presented as estimated marginal means (point estimate) and 95% confidence limits (error bars) adjusted for values measured after 3 h of heat exposure prior to the cooling intervention and corrected for multiple comparisons. Data were analyzed using linear mixed-effects models. The raw data used to create this figure are summarized in Table S2 in the supplemental materials. Note: CI, confidence interval; diff, difference; RH, relative humidity.

human thermoregulatory system.[10] Because this system operates in a negative feedback loop, cooling-induced reductions in core and skin temperatures suppress sweat secretion.[10,11] As a result, environmental heat gain is elevated upon return to the heat, causing body temperature and heat loss to increase in tandem until the rate of heat loss is sufficient to offset the rate of heat gain.[10,11] It follows that although increased heat loss is needed to prevent potentially dangerous levels of hyperthermia during heat stress, the accompanying elevation in body temperature is required to activate heat loss to an extent sufficient to do so.

Although we are, to our knowledge, the first to report on the transient nature of body cooling in the context of heat waves, ample research has assessed the effect of similar interventions in other contexts. For example, whole-body precooling is thought to benefit endurance exercise performance by delaying the development of hyperthermia.[73] However, Booth et al.[12] and Zimmerman et al.[13] observed that although precooling prior to cycling in the heat (~35°C) reduced core temperature by ~0.7–0.9°C, core temperatures in the precooling and control conditions converged by the end of the ~35 and ~40 min exercise bouts in the respective studies

Table 2. Cardiovascular function after the 2-h cooling intervention (hour 6) and at the end of the simulated heat wave (hour 9).

	Control [mean (SD)][a]	Cooling [mean (SD)][a]	Difference [mean (95% CI)][b]	p-Value[c]	ANOVA p-Values[d]		
					Group	Time	Interaction
Heart rate (bpm)					0.040	<0.001	<0.001
End of cooling intervention (hour 6)	81 (13)	71 (12)	−10 (−15, −6)	<0.001			
End of heat wave simulation (hour 9)	81 (15)	80 (14)	−1 (−4, 1)	0.58			
Change from cooling to end-simulation	0 (4)	9 (8)					
Rate pressure product (mmHg × bpm)					0.18	0.025	0.009
End of cooling intervention (hour 6)	9,508 (1,938)	7,945 (1,625)	−793 (−1,480, −106)	0.021			
End of heat wave simulation (hour 9)	9,438 (2,200)	8,815 (2,026)	147 (−540, 834)	>0.99			
Change from cooling to end-simulation	−70 (978)	870 (1,120)					
SDNN (ms)[e]					0.006	<0.001	<0.001
End of cooling intervention (hour 6)	37.4 (21.5)	47.8 (17.1)	12.5 (6.2, 18.8)	<0.001			
End of heat wave simulation (hour 9)	37.5 (19.1)	36.2 (18.3)	0.7 (−5.6, 7.0)	>0.99			
Change from cooling to end-simulation	0.1 (8.3)	−11.6 (9.6)					
RMSSD (ms)[e]					0.15	0.09	0.007
End of cooling intervention (hour 6)	22.7 (20.3)	22.5 (14.7)	5.4 (1.3, 9.4)	0.007			
End of heat wave simulation (hour 9)	24.2 (19.9)	18.1 (13.1)	−0.5 (−4.6, 3.5)	>0.99			
Change from cooling to end-simulation	1.5 (6.3)	−4.4 (6.1)					
Mean arterial blood pressure (mmHg)					0.19	0.18	0.08
End of cooling intervention (hour 6)	81 (8)	82 (7)	4 (−1, 8)	0.10			
End of heat wave simulation (hour 9)	84 (11)	82 (9)	1 (−4, 5)	>0.99			
Change from cooling to end-simulation	3 (5)	0 (5)					

Note: ANOVA, analysis of variance; CI, confidence interval; RMSSD, root mean square of successive differences; SD, standard deviation; SDNN, standard deviation of successive normal-to-normal RR intervals.
[a]Mean and SD of raw data for each index of cardiovascular function measured at the end of the cooling center intervention (hour 6) and the end of the heat wave simulation (hour 9) for the control ($n = 19$) and cooling groups ($n = 19$). The change from the end of the cooling intervention to the end of the simulation (unadjusted) is also presented.
[b]Estimated marginal mean difference and 95% CI derived from a linear mixed-effects model including fixed effects of group (control vs. cooling) and time (hours 6 and 9) and their interaction. Values for the analyzed outcome variable measured at the 3-h time point were also included as a covariate. Note that the mean difference, which is adjusted for responses measured prior to the cooling intervention, may not correspond to the mathematical difference between the summary data presented for the control and cooling groups (see footnote a). The 95% CI for each outcome is corrected for multiplicity using the Bonferroni procedure.
[c]p-Values for post hoc comparisons between control and cooling groups were adjusted for multiplicity using the Bonferroni procedure.
[d]p-Values are from the ANOVA for the linear mixed-effects models.
[e]Both heart rate variability indices (SDNN and RMSSD) were analyzed with a reduced sample size ($n = 18$ in control and cooling groups; missing data were not imputed).

due to a more rapid rate of bodily heating following precooling. Increased environmental heat gain secondary to cooling-induced reductions in skin temperature[12] and a delayed onset of sweating following precooling[12,13] are likely explanations for these observations. These studies thereby support the notion that the increase in body temperature during exposure to a given environment is physiologically determined[10,11]; ambient cooling is only effective for limiting hyperthermia for as long as it is applied.

Implications for Heat–Health Guidance

Based on the totality of experimental and observational evidence, visiting a cooling center or other air-conditioned location should be recommended as a first line of defense when home cooling is unavailable, particularly for those with reduced physiological tolerance to elevated temperatures (e.g., older adults)[3] for whom simple home-based cooling interventions (e.g., electric fans) are less effective.[70,71] Many cooling centers are also free to access, offering effective protection from hot weather for those without the means to own and operate home air-conditioning.[5] Increasing the deployment of cooling centers and reducing barriers to their use (e.g., accessibility, stigma that centers are only for "old people") are critical for better protecting vulnerable persons during hot weather and heat waves.[5]

Future guidance, however, should note that the physiological effects of cooling centers abate quickly, meaning that supplemental interventions may be required after returning to a hot environment (e.g., after returning home or for those without permanent shelter), especially when ambient temperature remains elevated late into the day or overnight.[75] Such strategies might include

Table 3. Circulating extracellular inflammatory markers and change in plasma volume at hour 9 of the simulated heat wave.

	Control [mean (SD)][a]	Cooling [mean (SD)][a]	Difference [mean (95% CI)][b]	p-Value[c]
Interleukin-6 (pg/mL)				
End of heat wave simulation (hour 9)	6.19 (2.91)	5.90 (3.39)	−0.52 (−1.31, 0.27)	0.19
Change from pre-exposure to end-simulation	0.19 (1.08)	−0.06 (0.29)		
Tumor necrosis factor-α (pg/mL)				
End of heat wave simulation (hour 9)	11.90 (9.85)	13.12 (11.98)	−0.34 (−1.94, 1.26)	0.67
Change from pre-exposure to end-simulation	0.30 (1.63)	0.00 (2.40)		
C-reactive protein (mg/L)				
End of heat wave simulation (hour 9)	0.35 (0.20)	0.35 (0.19)	−0.03 (−0.07, 0.01)	0.16
Change from pre-exposure to end-simulation	0.00 (0.04)	−0.03 (0.07)		
Plasma volume (%)				
Change from pre-exposure to end-simulation	−2.9 (4.0)	−2.2 (2.8)	0.4 (−1.8, 2.6)	0.71

Note: CI, confidence interval; SD, standard deviation.
[a]Mean and SD of raw data for each inflammatory marker were measured at the end of the heat wave simulation (hour 9), as well as the change in plasma volume from preexposure (baseline) levels for the control ($n = 13$ for interleukin-6 and tumor necrosis factor-α; $n = 17$ for C-reactive protein and plasma volume) and cooling groups ($n = 17$ for interleukin-6 and tumor necrosis factor-α; $n = 19$ for C-reactive protein and plasma volume). Missing data were not imputed.
[b]Estimated marginal mean difference and 95% CI were derived from a linear mixed-effects model including fixed effects of group (control vs. cooling) and covariates for sex and baseline values (i.e., value of each inflammatory marker measured prior to heat exposure; inflammatory markers) or sex only (change in plasma volume). Note that the mean difference, which is adjusted for included covariates, may not correspond to the mathematical difference between the summary data presented for the control and cooling groups (see footnote a).
[c]p-Values for between-group comparisons were derived from the linear mixed-effects models.

simple interventions to prevent excessive increases in home temperature during the day (e.g., external shading).[75] These can be combined with low-cost personal cooling behaviors, such as shirt wetting or simultaneous fan use and skin dousing, which are theoretically more effective at lower ambient temperatures.[4]

Limitations

A potential limitation was that this was a small study and we enrolled participants who had not been previously diagnosed with common chronic conditions influencing heat vulnerability (e.g., type 2 diabetes, heart disease) or taking prescription medications known to impair thermoregulatory function (e.g., beta blockers, anticholinergics).[2,3] This was an explicit design choice due to the time and resource intensive measurements employed (including direct air calorimetry[25]) and the fact that this was, to our knowledge, the first assessment of physiological responses in older adults during daylong heat exposure; previous studies have generally been limited to a maximum of 4 h (typically 2–3 h).[45,47–49,69,70,76–79] Because air-conditioning cools by facilitating the transfer of heat along the skin-to-environment temperature gradient, it is unlikely that our primary findings would have been altered had we recruited more vulnerable participants. Supporting this postulate, we recently observed that physiological responses did not differ between older adults with or without type 2 diabetes during a 3-h exposure to extreme heat (52°C heat index).[48] Regardless, larger confirmatory studies are needed to corroborate our findings and improve generalizability to more at-risk populations, including those with common chronic diseases such as heart disease or type 2 diabetes or taking medications that modify thermoregulatory function (e.g., see our upcoming trial, ClinicalTrials.gov identifier: NCT05274009).

Further, we employed a laboratory-based design to overcome difficulties in assessing the effectiveness of cooling centers using more traditional forms of public health research.[5] This meant that we were unable to evaluate the physiological impacts of heat stress occurring during travel to and from centers. Over half of visitors access cooling centers by walking or taking public transit.[80] Even light physical activity causes substantial increases in metabolic heat gain,[81] and elevated environmental temperatures and solar loading can be experienced on exposed walking routes[82] or when waiting at unsheltered transit stops.[83] Consequently, core temperature is likely higher before reaching cooling centers, and more rapidly elevated after leaving, compared with in our study. Relatedly, most individuals visit cooling centers midday, when outdoor temperature is highest (e.g., between 1200–1600 hours).[84] As such, the environmental temperature is likely cooler when participants leave cooling centers, although the level of heat stress experienced upon returning home can remain high into the evening and overnight[85] owing to suboptimal dwelling characteristics (e.g., poor design and insulation) and the availability (or lack thereof) of effective cooling strategies (e.g., air-conditioning).[66] Quantifying and mitigating the heat stress and strain experienced during travel to and from cooling centers and upon returning home represent important areas for future inquiry and opportunities for multidisciplinary study combining epidemiological, urban planning, and physiological research.[4] Such work is of particular importance given that individuals of lower socioeconomic status experience greater levels of travel-associated heat stress[86] and that the distance between public cooled locations and residential areas is predictive of heat-related mortality.[87]

Conclusions

We observed a robust reduction in body core temperature in older adults briefly exposed to air-conditioning during a 9-h simulated heatwave. Our findings provide important experimental support for national and international guidance on the effectiveness of cooling centers. However, we also found that the cooling-induced reductions in physiological strain were transient, a factor that should be considered in future guidance issued by health agencies. More broadly, this work adds to a growing body of research using laboratory-based heat wave simulations to evaluate the physiological impacts of personal cooling interventions. Heat wave simulations are a promising tool that can be used to complement more traditional forms of public health research and facilitate the development of evidence-based guidance for protecting vulnerable persons from extreme heat, particularly where more direct assessment has proven unfeasible or unethical.

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